

REMARKS

The claims are 31-43, with claims 31 and 32 being independent. Support for claims 38-43 and the amendment of claims 33 and 34 may be found in the specification at page 11, lines 22-42 and page 12, lines 21-23.

The Examiner has requested submission of a new Abstract, a substitute specification, the references from the IDS filed on 9/27/04 and selected references from the IDS filed on 10/10/06.

Applicants submit herewith a new Abstract and copies of some of the documents missing from the IDSs filed on 9/27/04 and 10/10/06. Copies of CA 2169231, GB 2341549, WO99/65906 and WO 00/63203 are being submitted in a new IDS.

Applicants note that the allegedly missing document, WO'157 (WO98/54157), was submitted to the office. It is seen on PAIR as the reference having 54 pages (8th reference above the NPL document list). If the Examiner was intending to refer to a document other than WO98/54157, Applicants respectfully request the Examiner to contact Applicants' undersigned attorney to expedite submission of that document.

Applicants were unable to find a document that corresponds to "GB'805." The Examiner may be referring to US 6,187,805, which was cited on the IDS filed 10/10/06. If the Examiner was intending to refer to a different document, Applicants respectfully request the Examiner to contact Applicants' undersigned attorney to expedite the submission process.

Applicants also submit herewith a substitute specification, together with a marked-up specification indicating all changes (by strikeout and underlining) to the originally filed specification. Applicants submit that the amendments to the specification do not add new matter.

The specification has been amended to include specification headings and recite the continuing data information. In addition, the description of the drawings has been moved from the end of the specification and inserted before the Detailed Description of the Invention.

The specification has also been amended to delete all of the Examples unrelated to the subject claimed invention – only original Examples E1, E2, E16, E51 and E52 (re-numbered as E1, E2, E3, E4 and E5, respectively) have been retained in the substitute specification. The specification has also been amended at page 3, line 26 and page 37, lines 27-32 (of the parent PCT application; Marked-Up specification at page 4, line 30 and page 46, line 27) to reconcile the recitation of the Examples (E#) with the Examples remaining in the case.

Descriptions of the intermediates D1, D2, D3, D4, D5, D6, D7, and D35 (D35 has been re-numbered as D8), have been retained in the specification; all other Descriptions have been deleted.

Alternate procedures for D4 and D6 have been retained and re-positioned to follow the first recitations of D4 and D6, respectively.

An obvious error has been corrected in the substitute specification. The term "-methyl-" has been added to the name of the chloro-ethyl-amino starting material recited in Description 1 and Example 1 (Alternative Procedure 1): *bis*-(2-chloroethyl)-amine hydrochloride has been changed to -- *bis*-(2-chloro-ethyl)-methyl-amine hydrochloride--. Applicants respectfully submit that one of ordinary skill in the art would understand, based on the general and specific synthetic methods described in the subject specification, the name of the product compounds (3-bromo-8-(4-*methyl*-piperazin-1-yl)-quinoline (D1) and 8-(4-*methyl*-piperazin-1-yl)-3-phenylsulfonylquinoline (E1)) and the reported NMR data, that the product compounds of D1 and E1 are N-methylated and that the chloro-ethyl-amino starting material used to make those compounds should contain an N-methyl group. Moreover, Applicants respectfully submit that one of ordinary skill in the art would not only recognize that the name provided for this starting material compound in the originally filed specification was in error, but would understand what the correct name of the compound should be. Applicants respectfully submit that correction of this obvious error by re-naming this starting material (all occurrences) does not constitute new matter. (M.P.E.P. 2163.07 and *In re Oda*, 170 U.S.P.Q. 268 (CCPA 1971)).

Applicants have conducted a review of the details of some of the experimental procedures provided in the substitute specification in view of available

information in original laboratory notebook(s). This review revealed some discrepancies between the reported experimentals and the notebook write-ups. For example, it was noted that the solvent used in Example 1, Alternative Procedure 1 (at page 25, line 40 to page 26, line 17), was inadvertently written in the original specification as *t*-butanol. In the substitute specification submitted herewith, the solvent for this example has been changed to --*n*-butanol--; support for this amendment may be found in the specification at page 8, lines 9-10 (and page 5, line 30 to page 6, line 6). In addition, it was noted that the characterizing data for crystalline Form I (see original Example 52, new Example 4) was obtained using sample material prepared from another batch of Form I crystals. The substitute specification has been amended to clarify that the characterizing data is for crystalline Form I.

Description 6, Example 1 (Alternative Procedure 2) and Example 2 (Alternative Procedure) were found to provide information (e.g., reactant weight/volume and/or reaction conditions) that was inconsistent with the laboratory notebooks. The specification has been amended as follows.

Example 1, Alternative Procedure 2 (procedure for reductive methylation) has been deleted and the remaining E1 Alternative Procedures (e.g., 1 and 3) have been re-labeled for clarity.

Example 2, Alternative Procedure (process for removing a Boc group and crystallization of an HCl salt), has been amended to cancel the reactant weights/volumes. The procedure in the original specification for Example 2, Alternative Procedure, appears to be a generalized procedure, based on a series of smaller batch experiments.

Description 6 (process for diazotization/iodination) has been amended in accordance with the general methods description provided at page 10, lines 1-13 to recite the organic reagents used in the diazotization/iodination reaction sequence described in original Description 6. An alternative diazotization/iodination procedure to prepare D6 was provided in the originally filed specification.

Other discrepancies were noted (e.g., relating to work-up and purification procedures, and reaction handling (e.g., providing cooling for exothermic reactions)) for which no changes to the specification have been made. For example, in

Description 4, the procedure in the specification does not indicate that in the final purification step, the Biotage flash column was first loaded with dichloromethane. For Description 5, the laboratory notebook does not contain a recitation of the extra step of cooling the reaction mixture in an ice bath, and for Example 1, Alternative Procedure 1, the laboratory notebook does not contain a recitation of the work-up conditions (cooling, extraction and drying). Additional discrepancies were noted in the description of the chromatography conditions used to purify D7 and E1 (D7: solvent system used was DCM (dichloromethane), followed by 1% MeOH/DCM, followed by 2% MeOH/DCM; E1: oil was dissolved in acetone, and eluted using acetone).

Applicants respectfully submit that because the above-noted Examples and Descriptions involve the conventional use of conventional reagents and/or routine experimental techniques to accomplish conventional transformations and/or purifications, none of the above-noted discrepancies would impair the ability of one of ordinary skill in the art to prepare the compounds of this invention without undue experimentation.

Claims 35-37 were rejected under 35 U.S.C. 112, second paragraph; claims 33-34 were rejected under 35 U.S.C. 112, first paragraph, and claims 31-32, and 35-37 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting. Applicants respectfully traverse each of these rejections.

To support the rejection of claims 35-37 under 35 U.S.C. 112, second paragraph, the Examiner alleges that the compound being claimed is the same, namely Form II, and that reciting individual properties is not seen to distinguish the scope. Applicants agree that the compound of claims 35-37 is the same Form II; however, Applicants respectfully submit that these claims are written in proper dependent form.

Claim 32, from which each of claims 35-37 depend, does not in any way limit the physical form of the claimed compound. In contrast, each of claims 35-37 defines a specific solid, crystalline form of the compound of claim 32. Accordingly, each of claims 35-37 is properly dependent from claim 32, because each claim further limits the scope of the claim from which it depends. In addition, because each of claims 35-37 defines a specific solid, crystalline form of the compound of

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claim 32 in terms of a different physical characterization (e.g., XRPD, Raman or IR), proof of infringement of each of these properly dependent claims is different.

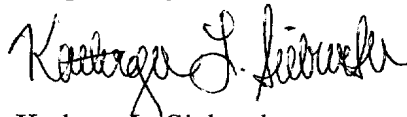
Claims 33-34 were rejected under 35 U.S.C. 112, first paragraph. Applicants have amended these claims in accordance with the Examiner's suggestion.

Withdrawal of these Section 112 rejections is respectfully requested.

Claims 31-32, and 35-37 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 13, and 21 of Application No. 10/509,077. This rejection is moot because U.S. Patent Application No. 10/509,077 is no longer co-pending (abandoned for failure to pay issue fee).

In view of the foregoing amendments and remarks, Applicants respectfully submit that the subject application is in condition for allowance. Applicants believe that they have addressed each of the Examiner's concerns and met each of the objections. If the Examiner has any remaining objections or concerns, the Examiner is respectfully requested to contact Applicants' undersigned attorney to resolve such issues and advance the case to issue.

Respectfully submitted,



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